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Pillsbury Winthrop LLP
Intellectual Property Group
11682 El Camino Real, Suite 200
San Diego, CA 92130-2593

EXAMINER

LE, EMILY M

ART UNIT	PAPER NUMBER
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1648

DATE MAILED: 03/10/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/910,483

Applicant(s)

FANG ET AL.

Examiner

Emily Le

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 02 December 2004.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,3-10,13,15-57 and 60-83 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1,3-10,13,15-57 and 60-83 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 7/19/01, 12/03/01, + 11/10/03 is/are: a) ☐ accepted or b) ☒ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____

DETAILED ACTION

Status of Claim(s)

1. Claims 2, 11-12, 14 and 58-59 are cancelled. Claims 1, 3-10, 13, 15-57 and 60-83 are pending and under examination.

Drawings

2. New corrected drawings are required in this application because "SEQ ID NO:" is not appended next to all instances of either amino acid or nucleic acid sequence listing. In addition, it is noted that the description of Figure 3 in the specification is not consistent with what is presented in Figure 3. Figure 3 presents the amino acids sequence of humanized 1A6 (HUM19), not HUMB. There is an inconsistency in the labeling. Applicant is advised to employ the services of a competent patent draftsman outside the Office, as the U.S. Patent and Trademark Office no longer prepares new drawings. The corrected drawings are required in reply to the Office action to avoid abandonment of the application. The requirement for corrected drawings will not be held in abeyance.

Applicant submits that replacement sheets for Figures 3 and 5 are provided with Applicant's 12/02/04 submission.

No replacement sheets can be found with Applicant's 12/02/2004 submission. As noted above, a lack of consistency in the naming of the antibodies is noted. The specification identifies the antibodies as Hum(A-D, F and H-I); yet, the drawings revert to a different form of identification for the antibodies, Hum(#) and Hs(#).

Specification

3. The disclosure is objected to because of the following informalities: newly submitted description for Figures 1 and 3 are not consistent with one another. The description provided for Figure 1 identifies SEQ ID NOs: 37 and 39 for murine 1A6 antibody and human consensus of heavy chain subgroup III (Humiii), and SEQ ID NOs: 38 and 40 for murine 1A6 antibody and human consensus of light chain subgroup III (Humiii), respectively. However, the same dedication of sequences is not noted in the description provided for Figure 3. The description provided for Figure 3 identifies SEQ ID NOs: 41 and 45 for murine 1A6 antibody and human consensus of heavy chain subgroup III (Humiii), and SEQ ID NOs: 42 and 46 for murine 1A6 antibody and human consensus of light chain subgroup III (Humiii), respectively.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

4. Claims 1, 3-10, 13, 15-57 and 60-83 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The claims are rendered indefinite for the following reason(s):

i) the recitation "non-human amino acid" and "human amino acid". It is unclear as to what is encompassed by "human" and "non human" amino acids. The art teaches that there are 20 common amino acids, however, the art does not differentiate between "human" and "non human" amino acids.

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ii) the recitation "framework region of the humanized antibody has had at least one non-human amino acid substituted with a human amino acid". The claimed invention is a "humanized antibody". The art recognizes that humanization of an antibody can be achieved by transplanting the combining site of the nonhuman antibody onto a human framework. Yet, the claims requires that the framework of the humanized antibody to have had at least one non-human amino acid substituted with a human amino acid, presuming that what is intended by "non-human" and "human" amino acid is directed at consensus sequences. If the claimed antibody is "humanized" using a technique that is art-recognized, then, it is unclear as to what is intended by Applicant with the cited recitation.

Furthermore, if Applicant intends specify that the claimed humanized antibody is a result of at least one amino acid substitution in the murine 1A6, then it is unclear, as to what is encompassed by Applicant's assertion of "humanized" antibody. As noted above, the art recognizes that humanization of an antibody can be achieved by transplanting the combining site of the nonhuman antibody onto a human framework; however, in the instant, Applicant requires amino acid substitution with in the framework region, which are based upon human consensus variable framework, with amino acid(s) that are based upon human consensus variable framework.

iii) claims 60-62 require that the framework region of the claimed antibody to be substituted with a specific number of amino acids, wherein the amino acids is based upon a human consensus variable framework region sequence.

In the instant, it is unclear as to what is intended by the cited limitation. The claimed antibody is a humanized antibody. The art recognizes that humanization of an antibody can be achieved by transplanting the combining site of the nonhuman antibody onto a human framework. Thus, since the claimed antibody is a humanized antibody, it is presumed that human framework is present. Ergo, it is unclear as to why the cited claims further specifies substitution of the amino acids, which is based upon a human consensus variable framework region sequence, be replaced with itself.

In addition to the above provided interpretation of the claims, the claims can also be interpreted as follow:

a) the claims are directed to specify the number of amino acids that has been substituted in the murine 1A6 to give rise to the claimed "humanized" antibody. If so, then it is unclear as to the exact number of substitution that the humanized antibody has had. Is it 1, 2, 3.... or 10 amino acids? Additionally, if this is what Applicant intends, then it is unclear as to what is encompassed by Applicant's assertion of "humanized" antibody. As noted above, the art recognizes that humanization of an antibody can be achieved by transplanting the combining site of the nonhuman antibody onto a human framework; however, in the instant, Applicant requires amino acid substitution with in the framework region, which are based upon human consensus variable framework, with amino acid(s) that are based upon human consensus variable framework.

b) the claims are directed to derivatives of the claimed humanized antibody, aside from the subsequences claimed. If this is Applicant's intention, then it is not readily apparent in the claims. Additionally, similar to the analysis provided above, the

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claimed invention is directed at a humanized antibody; thus, implicating the presence of a human framework. Ergo, it is unclear as to which amino acid(s) should be substituted, and amino acid(s) that can be used to replace the substituted amino acids; since both are based upon a human consensus variable framework region sequence.

iv) claims 63-83 require that the substituted antibody have a higher affinity to ICAM-1 than that of unsubstituted humanized antibody. In the instant, it is unclear what Applicant regards as the “substituted” and “unsubstituted” antibody. Independent claim 1 clearly specifies that the variable framework region of the claimed humanized antibody have had at least one substitution. Claim 4 further extrapolates on this limitation by clarifying that the substitution is based upon a human consensus variable framework region sequence. The claims does not give rise to another substituted antibody, other than the one that is instantly claimed—a humanized antibody that binds to ICAM-1 comprising SEQ ID NO: 5 and 7 (HumB). Ergo, without any apparent claim to other substituted antibody, it is unclear as to what is intended by these claims.

v) claims 48-52 are directed at a method of inhibiting HRV progression. It is unclear what is intended by “progression” of the virus. Is the recitation directed at the rate at which the virus replicates? Is the recitation directed at the rate at which the virus infects?

vi) the recitation “or a subsequence thereof. It is unclear if the claims are directed to i) a humanized antibody that comprises fragments of SEQ ID NOs: 5 and 7; or ii) fragments of the claimed humanized antibody which comprises SEQ ID NOs: 5 and 7.

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5. Claims 1, 4, 16-22, 25-57 and 60-83 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are directed to subsequence, fragments, of HumB.

The claims do not require that the fragments possess any particular distinguishing feature, biologic activity, or conserved structure. Therefore, the claims are drawn to a genus of fragments that are defined only by the identity of the fragments to the amino acid sequence of the humanized antibody, HumB.

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. In this case, the only factor present in the claims is the fragments are derived from HumB. Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the claimed genus, any fragments that can be derived from HumB.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of *the invention*. The invention is, for purposes of the

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'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116). As discussed above, the skilled artisan cannot envision the detailed chemical structure of the encompassed genus of fragments, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of making the antibody and its fragments. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of making the antibody and its fragments. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Therefore, only humanized antibody that binds to ICAM-1 comprising a VH domain consisting of SEQ ID NO: 5 and a VL domain consisting of SEQ ID NO: 7; and fragments thereof, wherein the fragments binds to ICAM-1; but not the full breadth of the claim meets the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

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~It is noted that Applicant has anticipated this rejection, since Applicant has incorporated the limitation of cancelled claim 2 into currently amended claim 1. In anticipation of this rejection, Applicant submits that HumB subsequences of claim 1 are defined structurally and functionally, while noting that HumB subsequences are defined by sequence, namely fragments of SEQ ID NOs: 5 or 7; and the subsequences are required to bind to ICAM-1.

Applicant's submission has been considered, however, it is not found persuasive. Contrary to Applicant's submission, the claims as presented do not i) limit the subsequences to just SEQ ID NO: 5 and SEQ ID NO: 7; and ii) require that the subsequences bind to ICAM-1. Additionally, the term "subsequence" encompasses a multitude of fragments that can possibly be derived from HumB. This interpretation of "subsequence" is in accordance with the definition that is provided by Applicant. The specification states, the term "subsequence" or "fragment" means a portion of the full-length molecule. For example, a subsequence of an antibody is one or more amino acid less in length than full-length polypeptide (e.g. one or more internal or terminal amino acid deletions from either amino or carboxy-termini). Subsequences therefore can be any length up to the full-length molecule.

6. Claims 1, 3-10, 13, 15-57 and 60-83 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

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Claims 1, 3-10, 13, 15-57 and 60-83: Support cannot be found for the following newly added limitation, "wherein a variable framework region of the humanized antibody has had at least one non-human amino acid substituted with a human amino acid".

Applicant submits that support for the recited limitation can be found at page 5, lines 15-19; page 34 lines 16 to page 36, line 18.

Applicant's submission has been noted, however, the cited support is not sufficient to provide adequate written description for the newly added limitation. The cited support has no reference to substitution of at least one non-human amino acid with a human amino acid.

Claims 71 and 82: Support cannot be found for the recitation of "50 to 100", line 2 of the claim. It is acknowledge that the specification teaches "...20- to 100-fold or greater than the parental antibody", however, such recitation do not support "50 to 100". Although the specification teaches a specific target range of 20-100 fold, there is no specific teaching of a species with the range. Therefore, "50 to 100" constitutes as new matter.

Applicant submits that in *In re Werheim*, the court held that because the specification disclosed a range of 25%-60%, the limitation "between 35%-60%" meets the written description requirement. Thus, in accordance with the court's position, Applicant submits that the adequate written description is provided for the instantly claimed invention.

Applicant's submission has been considered, however, it is not found persuasive. MPEP § 2163.05 [R-2], Range Limitation, states, "With respect to changing numerical

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range limitations, the analysis must take into account which ranges one skilled in the art would consider inherently supported by the discussion in the original disclosure. In the decision in *In re Werheim*, 541 F.2d 257, 191 USPQ 90 (CCPA 1976), the ranges described in the original specification included a range of "25%- 60%" and specific examples of "36%" and "50%." A corresponding new claim limitation to "at least 35%" did not meet the description requirement because the phrase "at least" had no upper limit and caused the claim to read literally on embodiments outside the "25% to 60%" range, however a limitation to "between 35% and 60%" did meet the description requirement. In the instant, the disclosure that is provided within the specification does not follow the same fact pattern as that presented in *In re Werheim*. In the instant, there is no evidence that would implicate that the claimed range is inherently supported by the original disclosure. Furthermore, the Examiner directs Applicant's attention to *In re Lukach*, 442 F.2d 967, 169 USPQ 795 (CCPA 1971)—wherein a subgenus range is found not to be supported by generic disclosure and specific example within the subgenus range; and *In re Smith*, 458 F.2d 1389, 1395, 173 USPQ 679, 683 (CCPA 1972)—wherein a subgenus is not necessarily described by a genus encompassing it and a species upon which it reads.

7. Claims 1, 4, 16-22, 25-57 and 60-83 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for HumB, and subsequences of HumB that binds to ICAM-1. The specification does not reasonably provide enablement for subsequences of HumB that does not bind to ICAM-1. The specification does not enable any person skilled in the art to which it pertains, or with

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which it is most nearly connected, to use the invention commensurate in scope with these claims.

To be enabling, the specification of a patent must teach those skilled in the art how to use the full scope of the claimed invention without undue experimentation. In *Genentech Inc. v. Novo Nordisk* 108 F.3d 1361, 1365, 42 USPQ2d 1001, 1004 (Fed. Cir. 1997); *In re Wright* 999 F.2d 1557, 1561, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993); See also *Amgen Inc. v. Chugai Pharm. Co.*, 927 F.2d 1200, 1212, 18 USPQ2d 1016, 1026 (Fed. Cir. 1991); *In re Fisher* 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). Further, in *In re Wands* 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988) the court stated:

Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized by the board in *Ex parte Forman* [230 USPQ 546, 547 (Bd Pat App Int 1986)]. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

Nature of the invention is directed antibodies.

The claims do not require that the fragments possess any particular distinguishing feature, biologic activity, or conserved structure; nor does the claims require that the regions that controls the binding specificity of the humanized antibody to be retained. Ergo, the breadth of the claims encompasses a multitude of fragments that can be derived from HumB.

The specification does not teach of fragments of HumB.

The specification does not contain any working examples of any fragments of HumB.

The specification does not limit fragments or subsequences to fragments of the antibody that comprises the regions that controls the binding specificity of the humanized antibody to be retained.

In the instant, the skilled artisan would not know how to make non-identical antibodies on the basis of teachings in the prior art or specification unless they possessed the noted activities--binds to ICAM-1, like the complete antibody in which the fragments are derived. The claims are unduly broad because they do not require the fragments to retain the CDR regions of the humanized antibody. The claims also do not require the fragments to possess a particular function.

It is well established in the art that the formation of an intact antigen-binding site generally requires the association of the complete heavy and light chain variable regions of a given antibody, each of which consists of three CDRs which provide the majority of the contact residues for the binding of the antibody to its target epitope. The amino acid sequences and conformations of each of the heavy and light chain CDRs are critical in maintaining the antigen binding specificity and affinity which is characteristic of the parent immunoglobulin. It is expected that all of the heavy and light chain CDRs in their proper order and in the context of framework sequences which maintain their required conformation, are required in order to produce a protein having antigen-binding function and that proper association of heavy and light chain variable regions is required in order to form functional antigen binding sites. Even minor changes

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in the amino acid sequences of the heavy and light variable regions, particularly in the CDRs, may dramatically affect antigen-binding function as evidenced by Rudikoff et al.¹ Rudikoff et al. teach that the alteration of a single amino acid in the CDR of a phosphocholine-binding myeloma protein resulted in the loss of antigen-binding function.

Thus, for these reasons set forth above, the claims are rejected under 35 U.S.C. 112, first paragraph, because the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected to use the invention commensurate in scope with these claims.

A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation. *In re Wright*, 999 F. 2d 1557, 1562, 27 USPQ 2d 1510, 1513 (Fed. Cir. 1993).

8. Claims 5-10, 13 and 16-57 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention.

Applicant submits additional information on how the one working example that is provided in the specification is carried out, and evidence showing that the cells used in

¹ Rudikoff et al. Single amino acid substitution altering antigen-binding specificity. Proc Natl Acad Sci

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the working examples is an established for use with HRV. Thus, in view of the submission, Applicant submits that claimed invention is enabling.

Applicant's submission has been considered, however it is not found persuasive. In accordance with Applicant's submission, in conjunction with the claimed antibody, the murine 1A6 antibody—the basis for the claimed antibody, should also be effective in inhibiting HRV infection. However, the contrary has proven itself. Charles et al. notes that in a receptor-blocking approach, murine 1A6 antibody prevents HRV infection, thereby inhibits HRV infectivity; however, in human clinical trials, contrary to the in vitro data gathered, the antibody failed to prevent onset of HRV infection.² Ergo, in view of the teaching of Charles et al., the working example provided fails to enable the skilled artisan to use the claimed invention without an undue burden of experimentation.

Claim Rejections - 35 USC § 103

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

10. Claims 1 and 3-4 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Colonno et al. and Padlan, for reason set forth in the previous office action.

Applicant submits that the claimed invention is patentable because:

SA, 1982, Vol 79, page 1979-1983, see abstract.

² Charles et al. Prevention of Human Rhinovirus Infection by Multivalent Fab Molecules Directed against ICAM-1. Antimicrobial Agents and Chemotherapy, 2003, 1503-1508.

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i) the combination of Colonno et al. and Padlan et al. fail to teach or suggest each and every element of the claimed humanized antibody, because they failed to teach or suggest a humanized antibody in which a variable framework region of the humanized antibody has had one or more non-human amino acids substituted with a human amino acid, let alone a human amino acid of a human consensus variable framework region sequence.

Applicant's submission has been considered, however, it is not found persuasive. To the contrary of Applicant's assertion, both Colonno et al. and Padlan et al. suggests and/or teaches humanized antibody; additionally, Padlan et al. teaches human consensus sequences. While Applicant is correct to note that neither suggests a humanized antibody in which a variable framework region of the humanized antibody has had one or more non-human amino acids substituted with a human amino acid, however, the submission cannot be considered on its merits because it is unclear as to what is intended by Applicant with the limitation, "...humanized antibody has had one or more non-human amino acids substituted with a human amino acid.

ii) Padlan teaches away from producing the claimed antibody because Padlan teaches retaining donor-antibody framework sequences in order to preserve antigen binding.

Applicant's submission has been considered, however, it is not found persuasive. It appears that Applicant has misconstrued the teaching of Padlan. Padlan does not teach retention of the donor-antibody (non-human) framework sequences in order to preserve antigen binding. Padlan provides a guideline as to factors that should be

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considered in producing a humanized antibody. Padlan is focused on reduction in the immunogenicity of the non-human antibody while preserving the antibody's antigen-binding properties. Ergo, contrary to Applicant's assertion, Padlan et al. does not teach away from the claimed invention.

Claim Rejections - 35 USC § 102

11. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

12. Claims 1 and 22 are rejected under 35 U.S.C. 102(b) as being anticipated by Pedersen et al. (U.S Patent No. 5639641).

The claims are directed to subsequences of claimed humanized antibody, wherein the claimed antibody comprises SEQ ID NO: 5 and SEQ ID NO: 7.

The specification defines subsequences as "...a portion of the full length molecule. For example, a subsequence of an antibody is one or more amino acid less in length than full length polypeptide (e.g. one or more internal or terminal amino acid deletions from either amino or carboxy-termini). Subsequences therefore can be any length up to the full length molecule."

Pedersen et al. teaches SEQ ID NO: 497, which is Arg Ala Ser Gln Ser Ile Ser Asn Asn Leu His. SEQ ID NO: 497 have 100% identity to a CDR region of the claimed antibody. SEQ ID NO: 497 is a fragment of the claimed antibody. Ergo, Pedersen et al. anticipates the claimed invention.

Conclusion

13. No claim is allowed.

14. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP

§ 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Emily Le whose telephone number is (571) 272 0903.

The examiner can normally be reached on Monday - Friday, 8 am - 5:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on (571) 272-0902. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



E. Le



Jeffrey S. Parkin, Ph.D.
Primary Patent Examiner
Art Unit 1648